

BIOGRAPHICAL SKETCH

NAME Keith A. Houck		POSITION TITLE Toxicologist	
eRA COMMONS USER NAME			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Guilford College, Greensboro, NC	B.S.	1980	Biology
University of North Carolina, Chapel Hill	M.S.	1982	Chemistry
Duke University, Durham, NC	Ph.D.	1989	Pathology/Toxicology
Genentech, Inc.	Post-doc	1989-1992	Molecular Biology

A. POSITIONS and HONORS**Research and Professional Experience:**

2006-present Toxicologist, National Center for Computational Toxicology, USEPA, NC
 2005-Present Lead Generation Team/Consultant, SAIC, NINDS Spinal Muscular Atrophy Project
 2005 Consultant, Dept. Cell and Tissues Engineering, Becton-Dickinson, RTP, NC
 1994-2004 Research Advisor, Lilly Research Laboratories, Eli Lilly & Co., RTP, NC.
 1992-1994 Senior Biologist, Sphinx Pharmaceuticals, RTP, NC.
 1982-1985 Senior Research Analyst, Pathology Department, Duke University

Professional Societies and Affiliations:

Society of Biomolecular Sciences
 Society of Toxicology
 AAAS

Honors and Awards:

2000 Changing the World Award, Eli Lilly & Co.
 2003 Best Paper Award, Society of Biomolecular Sciences

Selected Invitations at National & International Symposia:

EPA's ToxCast™ Program for Predicting Hazard and Prioritizing Toxicity Testing of Environmental Chemicals
 CASCADE Workshop on Synergies from Global Chemical Screening Programs (US-EPA/OECD) Oct. 1, 2007.
 Toxicity Profiling Using High-Throughput and High-Content Technologies. 13th Annual Conference of the Society of Biomolecular Screening, Montreal, Canada, April 15-19 2007.
 Environmental chemical hazard prediction by high-throughput screening and genomics approaches in the ToxCast program of the US Environmental Protection Agency. Fall Symposium of the National Capital Area Chapter Society of Toxicology, Bethesda, MD, Dec. 11, 2006.
 Methods for Evaluating Compounds as Ligands for the Human Xenobiotic Nuclear Receptor SXR. 9th Annual Conference of the Society of Biomolecular Screening, Portland, OR, Sept. 21-25, 2003.
 Protein: Protein Interactions as Novel Drug Targets. 8th Annual Conference of the Society of Biomolecular Screening, The Hague, Netherlands, Sept. 22-26, 2002.
 High-Throughput Screens Detection Protein:Protein and Protein:DNA Interactions Utilizing AlphaScreen™ Technology. 8th Annual Conference of the Society of Biomolecular Screening, The Hague, Netherlands, Sept. 22-26, 2002.
 Houck, KA, High-Throughput Screening Assays for Inhibitors of Cyclin-Dependent Kinases, IBC Conference on Regulation of the Cell Cycle, Boston, 1997 (invited).

Dixon J, D Bronson, NB Rankl, TM Gurganus, JW Rice, J Butler, R Beckmann, MS Kasher, Houck, KA
Expression, purification, and characterization of human cyclin D1/CDK4 from insect cells. Keystone
Symposia "The Cell Cycle": A139, Taos, NM, 1996.

Selected Expert Committees/Advisory Panels/Organizing Committees:

Lecturer, North Carolina Central University, 2007.

Chair, Toxicity Profiling Using High-Throughput and High-Content Technologies, Society of Biomolecular
Sciences, 2007.

Manuscript reviewer: EHP, DMD, J. Chem. Inf. Mod., ADDT 2006-2007.

Contributor to Risk Assessment of Engineered Nanomaterials proposal to EU 7th Framework Programme, 2007
NIH Study Section, Assay Development for High Throughput Molecular Screening, 2006.

Endowment Committee member, Society of Biomolecular Sciences, 2004-present.

Chair, Protein:Protein Interactions as Novel Drug Targets, Society of Biomolecular Sciences, 2003.

Juvenile Diabetes Research Foundation Grant Reviewer, 2006.

Teach Link Fellow, NC Science, Math and Technology Center, 2004-2007

Selected Assistance/Advisory Support to the Agency:

ORD Nanomaterials Research Strategy Team, 2007

TOCOR, Nine EPA contracts for ToxCast Program.

Project Officer, IAG with NIH Chemical Genomics Center, 2006-2007

Science Forum Session Co-chair, 2007

Chemical Prioritization Community of Practice Co-coordinator, 2006-present

EPA reviewer of OECD DRP: Use of Metabolising Systems for in vitro Testing of Endocrine Disruptors, 2007

B. SELECTED PUBLICATIONS (selected from 35 total).

Kavlock, RJ, G Ankley, J Blancato, M Breen, R Conolly, D Dix, K Houck, E Hubal, R Judson, J Rabinowitz, A
Richard, RW Setzer, I Shah, D Villeneuve, and E Weber. Computational Toxicology—A State of the
Science Mini Review. *Toxicol. Sci.*, *submitted*.

Houck, K.A. and R.J Kavlock. Understanding Mechanisms of Toxicity: Insights from Drug Discovery Research.
Toxicol.. Appl. Pharmacol., *in press*.

Dix, D.J., Houck, K.A., Martin, M.T., Richard, A.M., Setzer, W., and Kavlock, R.J. The ToxCast program for
prioritizing toxicity testing of environmental chemicals. *Toxicol. Sci.* 95:5-12, 2007.

Borchert KM, RJS Galvin, DR Nickischer, OJ Trask, Houck, KA. Screening for Activators of the Wnt/Fzd
Pathway by Automated Fluorescent Microscopy. *Methods Enzymol.* 414:140-50, 2006.

Schmidt RJ, JV Ficorilli, Y Zhang, KS Bramlett, TP Beyer, K Borchert, MS Dowless, KA Houck, TP Burris, PI
Eacho, G Liang, LW Guo, WK Wilson, GJ Schroeffer Jr, LF Michael, G Cao. A 15-keto sterol is a liver X
receptor ligand that suppresses sterol responsive element binding protein 2 activity. *J Lipid Res.*, 47:1037-
44, 2006.

Houck, KA, WP Bocchinfuso, MS Dowless, KM Borchert,. Reporter Gene Assays for Drug Discovery In: Minor,
L., ed., *Handbook of Assay Development in Drug Discovery*, pp. 357-370. New York: Marcel Dekker, Inc.,
2005

Borchert KM, RJS Galvin, CA Frolik, LV Hale, R Gonyier, OJ Trask, DR Nickischer, KA Houck. Phenotypic
screening for activators of the wnt/frizzled pathway in primary human osteoblasts. *Assay and Drug Dev.*
Technol. 3: 133-141, 2005.

Dowless MS, JL Barbee, KM Borchert, WP Bocchinfuso, KA Houck,. Cyclic AMP-independent activation of
CYP3A4 gene expression by forskolin. *European J. Pharmacol.* 512:9-13, 2005.

Burris TP, C Montrose, KA Houck, HE Osborne, WP Bocchinfuso, RW Zink, RJ Barr, CD Hepler, V Krishnan,
HA Bullock, LL Burris, RJ Galvin, K Bramlett, KR Stayrook, The hypolipidemic natural product
guggulsterone is a promiscuous steroid receptor ligand. *Mol Pharmacol* 67:948-954, 2005.

Houck KA, KM Borchert, CD Hepler, JS Thomas, KS Bramlett, LF Michael, TP Burris. T0901317 is a dual
LXR/FXR agonist. *Mol Genet Metab* 83:184-187, 2004.

Hamdouchi C, H Keyser, E Collins, C Jaramillo, JE De Diego, CD Spencer, JA Dempsey, BD Anderson, T
Leggett, NB Stamm, RM Schultz, SA Watkins, K Cocke, S Lemke, TF Burke, RP Beckmann, JT Dixon, TM

- Gurganus, NB Rankl, KA Houck, F Zhang, M Vieth, J Espinosa, DE Timm, RM Campbell, BKR Patel, HB Brooks. The discovery of a new structural class of cyclin-dependent kinase inhibitors, aminoimidazo[1,2-a]pyridines. *Mol Cancer Ther* 3: 1-9, 2004.
- Bettoun DJ, TP Burris, KA Houck, DW Buck II, KR Stayrook, B Khalifa, J Lu, WW Chin, S Nagpal, Retinoid X receptor is a non-silent major contributor to vitamin D receptor-mediated transcriptional activation. *Molecular Endocrinology*, 17:2320-2328, 2003.
- Bramlett KS, KA Houck, KM Borchert, MS Dowless, Y Zhang, TP Beyer, R Schmidt, R Barr, C Montrose, PI Eacho, G Cao, TP Burris. A natural product ligand of the oxysterol receptor, LXR *J. Pharmacol Exper.* 307:291-296, 2003.
- Graff JR, BW Konicek, AM McNulty, Z Wang, K Houck, S Allen, JD Paul, A Hbailu, RG Goode, GE Sandusky, RL Vessella, BL Neubauer. Increased AKT activity contributes to the prostate cancer progression by dramatically accelerating prostate tumor growth and diminishing p27Kip1 expression. *J. Biol. Chem.*, 275: 24500-24505, 2000.
- Skidmore BJ, NB Stamm, K Otto, S Kovacevic, SA Watkins, P Rutherford, S Lemke, K Cocke, RP Beckmann, K Houck, D Johnson, and RN Rao. Conditional transformation of rat embryo fibroblast cells by a cyclin D1-cdk4 fusion gene. *Oncogene* 18:6343-6356, 1999.
- Park JE, HH Chen, J Winer, KA Houck, N Ferrara. Placenta growth factor: Potentiation of vascular endothelial growth factor bioactivity, in vitro and in vivo, and high affinity binding to Flt-1 but not to Flk-1/KDR. *J. Biol. Chem.*, 269: 25646-25654, 1994.
- Kao J, K Houck, Y Fan, I Haehnel, S Libutti, M Kayton, T Grikscheit, J Chabot, R Nowygrod, S Greenberg, W-J Kuang, DW Leung, JR Hayward, W Kisiel, M Heath, J Brett, D Stern. Characterization of a novel tumor-derived cytokine: Endothelial-monocyte activating polypeptide II (EMAP-II). *J. Biol. Chem.*, 269:25106-25119, 1994.
- Kao J, Y-G Fan, I Haehnel, J Brett, S Greenberg, M Clauss, M Kayton, K Houck, W Kisiel, J Burnier, D Stern. A peptide derived from the amino terminus of endothelial-monocyte activating polypeptide II (EMAP II) modulates mononuclear and polymorphonuclear leukocyte functions, defines an apparently novel cellular interaction site, and induces an acute inflammatory response. *J. Biol. Chem.*, 269:9774-9782, 1994.
- Houck KA, DW Leung, AM Rowland, J Winer, N Ferrara. Dual regulation of vascular endothelial growth factor bioavailability by genetic and proteolytic mechanisms. *J. Biol. Chem.*, 267:26031-26037, 1992.
- Kim KJ, B Li, KA Houck, J Winer, N Ferrara. Vascular endothelial growth factor proteins: Identification of biologically relevant regions by neutralizing monoclonal antibodies. *Growth Factors*, 7:53-64, 1992.
- de Vries C, JA Escobedo, H Ueno, K Houck, N Ferrara, LT Williams. fms-like tyrosine kinase (flt) is a receptor for vascular endothelial growth factor (VEGF)/vascular permeability factor (VPF). *Science*, 255:989-991, 1991.
- Ferrara N, K Houck, L Jakeman, DW Leung. Molecular and biological properties of the vascular endothelial growth factor family of polypeptides. *Endocrine Rev.*, 13:18-32, 1991.
- Houck KA, N Ferrara, J Winer, G Cachianes, DW Leung. The vascular endothelial growth factor family: Identification of a fourth molecular species and characterization of alternative splicing of RNA. *Mol. Endocrinol.*, 5:1806-1814, 1991.
- Ferrara N, KA Houck, LB Jakeman, J Winer, DW Leung. The vascular endothelial growth factor family of polypeptides. *J. Cell. Biochem.*, 47:1-8 1991.
- Michalopoulos GK, R Zarnegar, K Houck, P Padiaditakis. Hepatopoietins A and B and hepatocyte growth. *Dig. Dis. Sci.*, 36: 681-686, 1991.
- Houck KA, R Zarnegar, SJ Muga, GK Michalopoulos. Acidic fibroblast growth factor (HBGF-1) stimulates DNA synthesis in primary rat hepatocyte cultures. *J. Cell. Physiol.*, 143: 129-132 1990.
- Houck KA, GK Michalopoulos. Altered responses of regenerating hepatocytes to norepinephrine and transforming growth factor type beta. *J. Cell. Physiol.*, 141: 503-509, 1989.
- Fendick EA, E. Mather-Mihaich, KA Houck, MB St. Clair, JB Faust, CH Rockwell, M Owens. Ecological toxicology and human health effects of heptachlor. *Reviews Environ. Contamination Toxicol.*, 111: 61-142, 1989.
- Houck KA, GK Michalopoulos, SC Strom. Introduction of a Ha-ras oncogene into rat liver epithelial cells and parenchymal hepatocytes confers resistance to the growth inhibitory effects of TGF-beta. *Oncogene*, 4: 19-25, 1989.

- Houck KA, JL Cruise, G Michalopoulos. Norepinephrine modulates the growth inhibitory effect of transforming growth factor beta in primary hepatocyte cultures. *J. Cell. Physiol.*, 135: 551-555, 1988.
- Cruise JL, KA Houck, G Michalopoulos. Early events in the regulation of hepatocyte DNA synthesis: The role of alpha-adrenergic stimulation. *Scandinavian J. Gastroenterology*, 23 (151): 551-555, 1988.
- Gebhardt R, JL Cruise, KA Houck, NC Luetke, A Novotny, F Thaler, G Michalopoulos. Differential effect of growth factors on growth stimulation and phenotypic stability of glutamine synthetase-positive and -negative hepatocytes in primary culture. *Differentiation*, 33: 45-55, 1986.
- Houck KA, G Michalopoulos. Proline is required for the stimulation of DNA synthesis in hepatocyte cultures by EGF. *In Vitro Cell. Dev. Biol.*, 21: 121-124, 1985.
- Cruise JL, KA Houck, G Michalopoulos. Induction of DNA synthesis in hepatocytes by norepinephrine via the alpha-1 adrenergic receptor. *Science*, 227: 749-751, 1985.
- Michalopoulos G, KA Houck, ML Dolan, NC Luetke. Control of hepatocyte replication by two serum factors. *Cancer Research*, 44: 4414-4419, 1984.